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EXAMINER	
ROMEO, D	
ART UNIT	PAPER NUMBER
1646	

DATE MAILED:
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Please find below a communication from the EXAMINER in charge of this application.

Commissioner of Patents

Office Action Summary	Application No. 08/443,982	Applicant(s) Dixit et al.
	Examiner David Romeo 3/8/98	Group Art Unit 1646

☒ Responsive to communication(s) filed on *Dec 8, 1997*.

☒ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-6, 21, 23, 24, 29-32, and 37-53* is/are pending in the application.

Of the above, claim(s) *53* is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-6, 21, 23, 24, 29-32, and 37-52* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☒ Claims *1-6, 21, 23, 24, 29-32, and 37-53* are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *17, 18*

☒ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Election/Restriction

1. Newly submitted claim 53 is directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: The method of claim 53 and the methods of claims 29 and 30 are independent and distinct, wherein each method performs different functions, using different starting materials and/or process steps. Furthermore, the product of claims 1-6, 21, 23, 24, 31, 32 and 37-52 and the method of claim 53 are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the product can be used in an immunization protocol for the production of antibodies.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claim 53 is withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

2. This application contains claim 53 drawn to an invention non-elected by original presentation. A complete reply to the final rejection must include cancellation of non-elected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Formal Matters

3. The Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1646.

4. The objection to the disclosure because of an informality is withdrawn in view of Applicants' amendment.

5. The objection to claim 23 because it depends from non-elected base claim 20 is withdrawn in view of Applicants' amendment.

6. Claims 2, 6, 21, 23, 24 and 46-52 are objected to because they depend from a non-elected base claim.

Drawings

7. The drawings are considered to be informal because they fail to comply with 37 CFR 1.84(a)(1) which requires black and white drawings using India ink or its equivalent.

Photographs and color drawings are acceptable only for examination purposes unless a petition filed under 37 CFR 1.84(a)(2) or (b)(1) is granted permitting their use as formal drawings. In the event applicant wishes to use the drawings currently on file as formal drawings, a petition must be filed for acceptance of the ***photographs*** or color drawings as formal drawings. Any such petition must be accompanied by the appropriate fee as set forth in 37 CFR 1.17(i), three sets of drawings or ***photographs***, as appropriate, and, if filed under the provisions of 37 CFR 1.84(a)(2), an amendment to the first paragraph of the brief description of the drawings section of the specification which states:

> The file of this patent contains at least one drawing executed in color. Copies of this patent with color drawing(s) will be provided by the Patent and Trademark Office upon request and payment of the necessary fee.

Color photographs will be accepted if the conditions for accepting color drawings have been satisfied.

Response to Arguments

8. The rejection of claims 1-6, 21, 23, 24 and 29-32 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for FADD proteins identified by SEQ ID NO:2,

does not reasonably provide enablement for a FADD protein, is withdrawn in part. The rejection of claims 1 and 3-5 is withdrawn in view of Applicants' amendment. The rejection of claims 2, 6, 21, 23, 24 and 29-32 is maintained for reasons of record. The rejection of record is applied to newly added claims 44 and 46-52. Applicants argue that the claims have been amended to recite structural limitations on FADD. Applicant's arguments have been fully considered but they are not persuasive because claims 2, 6, 21, 23, 24, 29-32, 44 and 46-52 have not been amended to recite any structural limitations on FADD. Furthermore, claim 44 is limited to a FADD protein comprising specific 5 to 15 amino acid peptides. The FADD polypeptide of the instant invention is 208 amino acids long. The usual expectation in the art would be that deleting 93 to 98% of a polypeptide's structure would result in a non-functional polypeptide. The specification has not shown that any one of the recited peptide fragments possesses FADD activity and the specification has not taught how to use a non-functional FADD. It is highly unpredictable as to whether the skilled artisan given any one of the recited peptides could make and use a functional FADD. There is no guidance provided in the specification other than SEQ ID NO:2 as to what amino acids may be added to the recited peptides such that a functional FADD polypeptide is obtained. The skilled artisan is left to perform extensive experiments wherein amino acid additions, insertions, substitutions, and deletions are made in a polypeptide comprising the recited peptides and through trial and error experimentation is left to identify which polypeptides have the properties of the instantly disclosed FADD polypeptide. Such trial and error experimentation is considered to be undue. Furthermore, it is not predictable that any of the recited peptides could

be used for the production of antibodies specific for the instantly disclosed FADD polypeptide. See Daniel et al. (U2) wherein it is taught that approaches to predicting antigenic epitopes based on primary amino acid sequence data were unsuccessful. Furthermore, these same approaches were unsuccessful at predicting known antigenic epitopes. Still further the antigenicity of any particular peptide was dependent upon the carrier (page 540, Abstract). In view of the breadth of the claims, the limited amount of direction and working examples provided by the inventor, the unpredictability in the art and the quantity of experimentation needed to make or use the invention based on the content of the disclosure, it would require undue experimentation for the skilled artisan to make and use the full scope of the claimed invention.

9. The rejection of claims 3-5 and 32 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for AU1-N-FADD and FADDmt, does not reasonably provide enablement for fragments of FADD, is withdrawn in part. The rejection of claims 3-5 is withdrawn in view of Applicants' amendment. The rejection of claim 32 is maintained for reasons of record. Applicants argue that the claims have been amended to recite structural limitations on FADD. Applicant's arguments have been fully considered but they are not persuasive because claim 32 has not been amended to recite any structural limitations on FADD.

10. The rejection of claims 29 and 30 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of screening for an agent that modulates the

binding of FADD of SEQ ID NO:2 to the intracellular domain of the Fas receptor, does not reasonably provide enablement for a method of screening for an agent useful to modulate cellular function regulated by the Fas receptor pathway, is maintained for reasons of record. Applicants argue that the claims have been amended to recite structural limitations on FADD. Applicant's arguments have been fully considered but they are not persuasive because claims 29 and 30 have not been amended to recite any structural limitations on FADD, and further because Applicants arguments do not address the rejection.

11. The rejection of claims 21, 23, 31 and 32 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, is withdrawn in part. The rejection of claims 21 and 23 is withdrawn in view of Applicants' amendment. The rejection of claims 31 and 32 is maintained for reasons of record. Applicants argue that it is well known to one skilled in the art that a "non-naturally occurring" protein or polypeptide is one that has not been purified or is not wild type. However, Applicants' argument is speculation and does not overcome the rejection. Applicants argue that examples of non-naturally occurring polypeptides include recombinantly produced proteins, analogs, variants and fusion proteins. However, all DNA is recombinant and all proteins are a result of recombination. Furthermore, analogs, variants, and fusion proteins all occur in nature. Applicants request the Office clarify the requirement that the claim provide a standard by which it could be determined whether a protein or polypeptide is naturally or non-naturally

occurring. In response to Applicants' request, the structural limitations of "FADD" are not clear and encompass any structure that has the desired biological activity. In view of a claim to a "non-naturally occurring" compound, wherein the structural limitations of the compound are not clearly set forth, it is impossible to tell if the claimed compound is a natural or non-natural compound. The metes and bounds of the claim are not clearly set forth. Amending the claim to recite "of any of claims 1 and 3-5" after "protein", would overcome the rejection.

12. The rejection of claims 1 to 5 and 31 to 32 under 35 U.S.C. 102(b) as being anticipated by Itoh (T, cited in previous Office action), is withdrawn in part. The rejection of claims 1 and 3-5 is withdrawn in view of Applicants' amendment. The rejection of claims 2, 31 and 32 is maintained for reasons of record. The rejection of record is applied to amended claims 6, 21, 23 and 24 and to newly added claims 46-49. Applicants argue that Itoh et al. does not disclose Applicants' protein or polypeptide, that the specification clearly discloses that the claimed FADD protein or polypeptide is not the intracellular domain of the Fas receptor nor an extracellular ligand of the Fas receptor, and that the newly amended claims clearly distinguish Applicants' FADD from the polypeptide disclosed by Itoh et al. Applicant's arguments have been fully considered but they are not persuasive. There are no structural limitations to the claimed protein and the Fas receptor disclosed by Itoh et al. al. meets all the structural and functional limitations of the claimed FADD protein. Although the Fas receptor disclosed by Itoh et al. al. and the claimed FADD protein are different in name, the specification specifically intends the term "FADD protein" to encompass

analogs of FADD (Specification, page 14, lines 15-18). The Fas protein disclosed by Itoh et al. al. is such an analog.

13. The rejection of claims 6, 23 and 24 under 35 U.S.C. 102(b) as being anticipated by Itoh et al. al. (U1), is withdrawn in part. The rejection of claims 23 and 24 is withdrawn in view of Applicants' amendment. The rejection of claim 6 is maintained for reasons of record. The rejection of record is applied to newly added claims 50 and 51 Applicants argue that Itoh et al. does not disclose Applicants' protein or polypeptide, that the specification clearly discloses that the claimed FADD protein or polypeptide is not the intracellular domain of the Fas receptor nor an extracellular ligand of the Fas receptor, and that the newly amended claims clearly distinguish Applicants' FADD from the polypeptide disclosed by Itoh et al. Applicant's arguments have been fully considered but they are not persuasive. There are no structural limitations to the claimed protein and the Fas receptor disclosed by Itoh et al. al. meets all the structural and functional limitations of the claimed FADD protein. Although the Fas receptor disclosed by Itoh et al. al. and the claimed FADD protein are different in name, the specification specifically intends the term "FADD protein" to encompass analogs of FADD (Specification, page 14, lines 15-18). The Fas protein disclosed by Itoh et al. al. is such an analog. Itoh et al. also disclose the Fas receptor and a carrier, wherein the carrier is a solid support (page 241, column 2, full paragraph 8).

14. The rejection of claim 21 under 35 U.S.C. 103(a) as being unpatentable over Itoh et al. al. (U1) in view of Berg et al. al. (A), is maintained for reasons of record. The rejection of record is applied to amended claim 23. Applicants argue that there is no suggestion or enablement for the invention of amended claim 21. Applicant's arguments have been fully considered but they are not persuasive. The Fas receptor is protein or polypeptide that meets the structural and functional definition of a FADD protein or polypeptide for reasons of record. The invention remains *prima facie* obvious over the prior art.

Claim Rejections - 35 USC § 112

15. Claims 3, 6, 21, 23, 41, 44, 45, 47-49 and 51 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claims 3, 6, 21, 23 and 47-49 recite the limitation "comprising amino acid 24 to amino acid 208". Support for this limitation cannot be found in the specification. Claim 41 recites the limitation "comprising amino acid 41 to amino acid 117". Support for this limitation cannot be found in the specification. Claim 44 recites the limitation "amino acids 111 to 116, 140 to 144, 146 to 160, 164 to 178, and combinations thereof". Support for this limitation cannot be found in the specification. Claim 45 recites the limitation "having conservative amino acid substitutions at amino acids 1 to 120 and 123 to 208". Support for this limitation cannot be found in the specification. Claims 49

and 51 recite the limitations "stabilizer" and "preservative". Support for this limitation cannot be found in the specification.

16. Claims 1-6, 21, 23, 24, 29-32, and 37-53 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the recited FADD polypeptides that retain FADD activity, i.e. bind the cytoplasmic region of the Fas receptor or induce apoptosis in a cell, and compositions comprising said FADD, does not reasonably provide enablement for the recited FADD polypeptides and compositions without regard to the functional activity of the encompassed polypeptides. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. The claims encompass FADD polypeptides with an unlimited number of conservative amino acid substitutions. Because the effects of mutations are cumulative, it is unlikely that the FADD proteins of the instant invention can tolerate an unlimited number of amino acid substitutions and retain their functional activity. It is also likely that there are an large number of inoperable embodiments, which the specification has not taught how to use absent undue experimentation. In view of the breadth of the claims and the quantity of experimentation needed to make or use the large number of inoperable embodiments of the invention, it would require undue experimentation for the skilled artisan to make and use the full scope of the claimed invention. It is suggested that the claims be limited to the recited FADD polypeptides that bind the cytoplasmic region of the Fas receptor or induce apoptosis in a cell

17. Claims 2, 37-44, 49 and 51 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 2 recites the limitation "mammalian protein" in line 1. There is insufficient antecedent basis for this limitation in the claim.

Claims 37-43 recite the limitation "fragment" in line 1. There is insufficient antecedent basis for this limitation in the claim. It is suggested that the claims recite -- a polypeptide fragment of the protein of claim 1--

Claim 44 is indefinite because the claim recites specific amino acid sequences without reciting an appropriate sequence identifier, i.e. SEQ ID NO:. Whenever, particular amino acid residues in a sequence are referred to the reference is meaningless without the appropriate SEQ ID NO:.

While applicant may be his or her own lexicographer, a term in a claim may not be given a meaning repugnant to the usual meaning of that term. See *In re Hill*, 161 F.2d 367, 73 USPQ 482 (CCPA 1947). The term "detectable label" in claims 49 and 51 is used by the claims to mean "carrier", while the accepted meaning is "an object serving as a means of identification." The accepted meaning of "carrier" is "one that transports or conveys".

Claim Rejections - 35 USC § 103

18. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

19. Claims 2 and 46 are rejected under 35 U.S.C. 103(a) as being unpatentable over Itoh (T) as applied to claim 2 above, and further in view of Sambrook et al. (V2). The Fas protein disclosed by Itoh et al. meets all the structural and functional limitations of a FADD polypeptide, for reasons of record and incorporated herein by reference. Itoh et al. do not disclose a fusion polypeptide comprising the Fas receptor. Sambrook et al. discloses the production of fusion proteins and discloses that fusion proteins are more stable and easier to identify (page 17.3). Sambrook et al. do not disclose a fusion protein of the Fas receptor. However, it would have been obvious to one of ordinary skill in the art at the time of Applicants' invention to produce a fusion protein of the Fas receptor, as taught by Sambrook et al., with a reasonable expectation of success. One of ordinary skill in the art would be motivated to combine these teachings because fusion proteins are more stable and easier to identify. The invention is prima facie obvious over the prior art.

20. Claims 6 and 52 are rejected under 35 U.S.C. 103(a) as being unpatentable over Itoh et al. al. (U1) as applied to claim 6 above, and further in view of Sambrook et al. (V2). Itoh et al. al. disclose a Fas receptor which has been recombinantly produced and isolated from a host cell

(Figure 3, page 236). The Fas receptor is protein or polypeptide that meets the structural and functional definition of a FADD protein or polypeptide for reasons of record and incorporated herein by reference. Itoh et al. do not disclose said Fas receptor wherein the host cell is a procaryotic cell. Sambrook et al. disclose the recombinant production of proteins in bacteria and disclose that expressing large amounts of protein from a cloned gene introduced into *E. coli* have proven invaluable in the purification, localization, and functional analysis of proteins (page 17.1-17.44). Sambrook et al. do not disclose the recombinant production of the Fas receptor. However, it would have been obvious to one of ordinary skill in the art at the time of Applicants' invention to recombinantly produce and isolate from a host cell a Fas receptor, as taught by Itoh et al., and to modify that teaching by recombinantly producing and isolating the Fas receptor from a prokaryotic cell, as taught by Sambrook et al., with a reasonable expectation of success. One of ordinary skill in the art would be motivated to combine these teachings in order to purify, localize, and functionally analyze the Fas receptor. The invention is prima facie obvious over the prior art.

Conclusion

21. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David S. Romeo whose telephone number is (703) 305-4050. The examiner can normally be reached on Monday through Friday from 8:00 a.m. to 4:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Stephen Walsh, can be reached on (703) 308-2957.

Official papers filed by fax should be directed to (703) 308-4242. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Elizabeth C. Kemmerer

ELIZABETH C. KEMMERER
PATENT EXAMINER

DSR DSR
March 8, 1998